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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/528,742	03/20/2000	Paul Roben	11390-002001	5781

20995 7590 11/26/2002

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EXAMINER	
WOITACH, JOSEPH T	
ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 11/26/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

File

Office Action Summary

Application No.	Applicant(s)
09/528,742	Roben et al.
Examiner	**Art Unit**
Joseph Woitach	1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Sep 10, 2002* .

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-55* is/are pending in the application.

4a) Of the above, claim(s) *12, 14, 15, 31, and 33-35* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-11, 13, 16-30, 32, and 36-55* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☒ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 15
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

This application filed March 20, 2000, claims benefit to provisional application 60/139,579, filed June 17, 1999.

Applicants amendment, filed September 10, 2002, paper number 16, has been received and entered. The specification has been amended.

Claims 1-55 are pending. Claims 12, 14, 15, 31 and 33-35 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a non-elected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 10. Claims 1-11, 13, 16-30, 32 and 36-55 are currently under examination as they are drawn to the elected species:(a) a sulfo-NHS ester moiety ; (b) a biotin binding domain; and (c) dithiopropionate.

This application contains claims drawn to an invention nonelected with traverse in Paper No. 10. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any

amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Specification

The disclosure objected to because the brief description of each of the drawing(s) must be present in the disclosure and because it contains an embedded hyperlink is withdrawn.

Amendments to the specification has obviated the basis of the objection.

The amendment filed September 10, 2002, paper number 16, is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: the amendment to the specification in the claim for priority includes the phrase "the disclosure of which is incorporated herein by reference in its entirety", however this was not recited or part of the original disclosure.

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Objections

Claims 1, 11, 19, 30, 51 and 52 stand objected to because the claims recite and encompass species which were not specifically elected.

Applicants note that claims subject to a species election will only be restricted if no generic claim is found allowable, citing MPEP 809.02. Further, upon finding a generic claim allowable, Applicants are entitled to consideration of claims to additional species, therefore argue that amendment to only the elected species is not required. See Applicants' amendment, bridging pages 3-4. Applicants arguments have been fully considered but not found persuasive.

As noted previously, Applicants have elected the species for each domain as set forth in claim 55 as: (a) a sulfo-NHS ester moiety ; (b) a biotin binding domain; and (c) dithiopropionate Examiner acknowledges Applicants' summary of restriction practice for an election of species, however it is noted that a generic claim has not been found allowable. Further, as set forth below, the claims as they are drawn to the elected species are not found allowable. Therefore, because the elected species and a generic claim has not been found allowable, the objection is maintained.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 52-54 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one

skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants point to the bridging paragraph on pages 20-21 for a description of the terms subject to the rejection and to the working example 1 as an example of limitations of what can be contained in the printed matter for practicing a method. Applicants argue that in light of the teaching in the instant application, the terms "kit" and printed matter" meet the written description requirements required by 35 USC 112, first paragraph. See Applicants' amendment, pages 4-5. Applicants arguments have been fully considered but not found persuasive.

The courts have stated that possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. *Pfaff v. Wells Electronics, Inc.,* 48 USPQ2d 1641, 1646 (1998). Examiner notes the examples provided by the present disclosure, however it is maintained that the specification fails to adequately describe the other necessary components of 'a kit' or the information contained in the 'printed matter' for practice of any of the claimed methods encompassed by the instant claims with particularity to indicate that Applicants had possession of the claimed invention because essential and critical elements are not adequately described in the specification. It is acknowledged that the specification recites the "instructions for practicing the methods of the invention, as set forth herein" (page 20) however there are no specific method steps or detailed listing of the components of a kit

specifically set forth which would be included on the printed matter. The instant disclosure provides general guidance for the generation and use of impermeable reagents, however it fails to set forth the specific reagents or specific 'instructions' which would be specifically included in a kit. Further, the intended use of the kit is specifically drawn to use in an intact organ however the specification fails to clearly set forth the specific buffers and reagents, or provide specific method steps for the practice of method as instantly claimed. In the instant case, the general guidance fails to provide the necessary description of the materials contained in a kit or what is specifically recited on the printed matter such as the specific method steps which may be used in practicing any particular method. The skilled artisan cannot envision what the specific reagents are to be included in the kit or what the specific printed matter indicates or recites, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method. Thus, while the present disclosure may provide the general guidance to practice the instantly claimed methods, it fails to provide the specific details for each of the reagents to be included in a kit for practice of a particular method, and fails to set forth specific instructions for each of the methods which would be included in the written material, and therefore, the rejection is maintained.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2, 17, 18, 20, 37 and 38 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention is withdrawn.

Applicants argue the claims are clear and definite as written, noting the courts have held the test for definiteness turns on what of one of skill in the art would understand the limitation to encompass in light of the specification, citing *In re Dossel*. Further, it is noted that the purpose of the claim is to legally define the metes and bounds of the property rights, and that the invention is enabled by the specification not the claims. See Applicants' amendment, page 5. Applicants arguments have been fully considered and found persuasive.

It is noted that the independent claim is drawn to identifying molecules which are non-specifically bound to the impermeable reagent, however Examiner would agree that among all the molecules that may be identified non-specifically by practicing the method, specific molecules would be present. The limitations of the claims are definite in that they set forth the metes and bounds of the dependent claim, and though the molecule is identified non-specifically, the specific molecules such as 'an organ-specific or a tissue-specific molecule', a polypeptide, and 'a lipid or a carbohydrate' would be present among the various molecules present on the cell surface of a cell.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -.
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 52 and 53 stand rejected under 35 U.S.C. 102(b) as being anticipated by Pierce Catalog & Handbook, 1994-95.

Applicants point out that the Pierce catalog does not indicate to administer the reagent "into the lumen" and thus, does not anticipate the claims. See Applicants' amendment, page 6. Applicants arguments have been fully considered and not found persuasive.

As noted previously, claims 52 and 53 encompass a kit comprising a impermeable reagent comprising the three domains: (a) a sulfo-NHS ester moiety ; (b) a biotin binding domain; and (c) dithiopropionate and printed matter instructing for the use of the reagent. Further, the limitation of the "administration into a lumen" is being interpreted as an intended use and thus, is not seen as providing patentable weight to the claimed invention. In support of this interpretation the CAFC in *In re Gulack* 217 USPQ 401 1983 stated that printed matter that is not functionally related to the substrate does not distinguish the invention from the prior art in terms of patentability (page 401). The court further stated that the critical question is whether there exists any new and unobvious functional relationship between the printed matter and the

substrate (page 404 "B"). In the instant case, the printed material would not affect any inherent property of the impermeable reagent. Additionally, the CAFC in *In Re Woodruff* 16 USPQ2d 1934 indicated that new uses for old compounds does not necessarily provide patentability to the old compound. The court, in replying to arguments of *In re Shetty* 195 USPQ 753 and *In Re Marshall* 198 USPQ 344, indicates that for new uses for old or obvious compounds to be patentable the claimed uses must be "completely new". In this context, Applicants' impermeable reagent is not disclosed as having a "completely new" use beyond being capable of labeling molecules present on a cell surface which was well known in the art at the time of filing. Finally, it noted is noted that the subject matter of the invention or discovery must come within the boundaries set forth by 35 U.S.C. 101, which permits patents to be granted only for "any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof." With regards to printed material, MPEP 706.03(a) indicates that a mere arrangement of printed matter, though seemingly a "manufacture," is rejected as not being within the statutory classes. See *In re Miller*, 418 F.2d 1392, 164USPQ 46 (CCPA 1969); *Ex parte Gwinn*, 112 USPQ 439 (Bd. App. 1955); and *In re Jones*, 373 F.2d 1007, 153 USPQ 77 (CCPA 1967).

As set forth in the previous rejection, the Pierce Catalog & Handbook teaches sulfosuccimidyl 2-(biotinamido) ethyl-1,3-dithiopropionate (NHS-SS Biotin) which is a reagent comprising (a) a sulfo-NHS ester moiety ; (b) a biotin binding domain; and (c) dithiopropionate (product number 21331; page T-131), and therefore provides both the reagents and kits, and the

general guidance for use of each of these in the purification of a protein present on the surface of a cell, and thus, anticipates the kit set forth in claims 52 and 53. Therefore, for the reasons above and of record, the rejection is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-11, 13, 16-30, 32 and 36-55 stand rejected under 35 U.S.C. 103(a) as being unpatentable over De La Fuente *et al.* (IDS reference), Hastie *et al.* (IDS ref)., and Rothschild *et al.* (US Patent 5,948,624) and the Pierce Catalog & Handbook, 1994-95.

Applicants summarize separately each of the teachings of De La Fuente *et al.*, Hastie *et al.*, and Rothschild *et al.* in light of the compounds disclosed in the Pierce catalog and argue that none references and the compounds taught in Pierce make obvious the instantly claimed method

or compositions. See Applicants' amendment, pages 6-9. Applicants arguments have been fully considered and not found persuasive.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). As set forth in the previous rejection, at the time of filing the compound sold by Pierce was disclosed as useful for labeling molecules on the surface of a cell. Each De La Fuente *et al.* and Hastie *et al.* teach to use a similar labeling compound, NHS-LC-biotin, for the identification and isolation of the particular components from the perfusiable space within an organ and on a tissue. Rothschild *et al.* was cited for a general description of heterobifunctional crosslinkers and for their use for the detection and isolation of biomolecules to identify and detect specific conjugates associated with a tissue that can be further used in determining the role of the molecule in the detection of disease or disorders. Clearly, at the time of filing, the labeling of tissues was being practiced and the use of heterobifunctional cross-linkers in these methods was known and practiced. Further, De La Fuente *et al.* clearly states that the methodology can be used to identify molecules on the luminal surface of a cell (see summary in abstract). Applicants' argument that administering the reagent to an intact organ is unobvious is unpersuasive because De La Fuente *et al.* clearly indicates that the methods are for identifying proteins accessible *via* the circulation. Additionally, with respect to Applicants' arguments that De La Fuente *et al.* does not provide a

reasonable expectation of success to use a cleavalbe reagent, it is noted that obviousness does not require absolute predictability of success; for obviousness under 35 U.S.C. § 103, all that is required is a reasonable expectation of success. See *In re O'Farrell*, 7 USPQ2d 1673 (CAFC 1988). In the instant case, Examiner agrees that De La Fuente *et al.* alone does not provide an expectation of success, however the teachings of De La Fuente *et al.*, Hastie *et al.*, and Rothschild *et al.* taken as a whole clearly teach the use of heterobifunctional cross-linker for labeling molecules on the cell surface of a cell, and that these methods were successfully practiced previously with other cross-linking reagents.

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to use the specific methods of De La Fuente *et al.* and Hastie *et al.* and those more general disclosed by Rothschild *et al.* with the cleavable cross-linkers for sale and discussed in the Pierce Catalog & Handbook.

Thus, for the reasons above and of record, the claims are *prima facie* obvious, and therefore, rejection is maintained.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (703)305-3732.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (703)305-4051.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (703) 308-2141.

Deborah Crouch

Joseph T. Woitach

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PRIMARY EXAMINER
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